Citation:

Kontogianni MD, Panagiotakos DB, Chrysohoou C, Pitsavos C, Stefanadis C. Modelling dairy intake on the development of acute coronary syndromes: The CARDIO2000 study. *Eur J Cardiovasc Prev Rehabil*. 2006 Oct; 13 (5): 791-797.

PubMed ID: 17001220

Study Design:

Case Control Study

Class:

C - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To evaluate the association between dairy consumption and the prevalence of a first, non-fatal event of an acute coronary syndrome, in a Greek sample.

Inclusion Criteria:

Cases

- First event of acute myocardial infarction (MI) diagnosed by two or more features such as typical electrocardiographic changes
- Compatible clinical symptoms and specific diagnostic enzyme elevations
- First diagnosed unstable angina corresponding to class III of the Braunwald classification.

Controls

- Age
- Sex
- Region-matched to cases.

Exclusion Criteria:

- None specified for Experimental Subjects
- Matching Control Subjects: No clinical symptoms or suspicion of CVD in their medical history.

Description of Study Protocol:

Recruitment

- Cases: Participants with a first symptom of coronary heart disease (CHD) were randomly selected from hospitals
- Controls: Age-, sex-, and region-matched randomly selected subjects who were mainly patients who visited the outpatients department of the same hospital and at the same period as the cases, for routine examinations or minor surgical operations. In a few cases, friends or colleagues of the cases were enrolled.

Design

Case-control study: CARDIO2000 is a multi-center case-control study with sampling from 10 Greek regions.

Dietary Intake/Dietary Assessment Methodology

Semi-quantitative food-frequency questionnaire (FFQ)

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Contingency tables with calculation of chi-square test evaluated associations between the categorical variables, while using the Student's T-test we evaluated the associations between groups of study and continuous variables
- The estimates of the odds ratios of having ACS were performed by calculating odds ratios (OR) and their corresponding 95% CIs through conditional logistic regression analysis. First the authors evaluated all the interactions between the exposure variables and the main factor of interest (dairy consumption). Afterwards, the authors explored the potential confounding effect of the other exposure variables (by adding and removing each one from the model)
- Both elimination procedures were based on the Wald's statistic.
- Significant confounders, as well as interactions were retained in the model
- Deviance residuals were calculated in order to evaluate the model's goodness-of-fit
- Cut-off point analysis was used in order to determine the optimal value of the weekly dairy products intake that differentiates patients from controls
- All reported P-values are two-sided and compared to a significance level of 5%.

Data Collection Summary:

Timing of Measurements

- Cases: Lifestyle characteristics obtained through questionnaire during an interview by a physician, after the second day of hospitalization
- Controls: Questionnaires completed at entry to study.

Dependent Variables

First, non-fatal event of an acute coronary syndrome (MI or unstable angina).

Independent Variables

Dairy intake (portions per week).

Control Variables

- Smoking
- Physical activity
- Education level
- Hypertension (HTN)
- Hypercholesterolemia
- Diabetes
- Presence of premature CHD among first-degree relatives
- Height/weight (BMI).

Description of Actual Data Sample:

- *Initial N:*
  - 700 male and 148 female cases
  - 830 male and 248 female population-based age and sex matched controls
- *Attrition (final N):* Same
- *Age:* Approximately 60±10 years
- *Ethnicity:* Natives of 10 Greek regions
- *Other relevant demographics:* Cases were more likely to have HTN, hypercholesterolemia, diabetes, be smokers, and physically inactive
- *Anthropometrics:* BMI: Approximately 27±4kg/m^2
- *Location:* Greece.

Summary of Results:

Key Findings

- An inverse relationship was observed between dairy products consumption and odds of having acute coronary syndrome. One portion increase in weekly dairy products intake was associated with 12% lower likelihood of having acute coronary syndrome, after controlling for BMI, smoking and dietary habits, physical activity level, educational status, as well as the presence of family history of CHD, hypertension, hypercholesterolemia, diabetes, and any special mediation used by the participants ($P<0.001$)
- Cut-off analysis showed that 7.4 portions per week are the optimal consumption that benefits people from having acute coronary syndrome.

Other Findings

- 98% of participants reported that they consume at least one portion of dairy products on a weekly basis
- Food-specific analysis showed that compared to no intake, yellow and white cheese consumption was associated with 23 and 53% lower odds of ACS, respectively (OR=0.77, $P<0.001$ and OR=0.47, $P<0.001$); yogurt intake was associated with 39% lower odds of ACS (OR=0.61, $P<0.001$); and low fat dairy products seem to confer more protection: 59% lower likelihood of having cardiac events (OR=0.41, $P<0.001$), after adjusting for age and sex of the participants

- Milk intake was not associated with the likelihood of having ACS, when other characteristics of the participants were taken into account (OR=1.16, P=0.12). However, patients and controls that consumed milk were older than those who did not consume (62±12 vs. 57±11, P<0.001) and were more likely to have diabetes (P=0.022) and hypercholesterolemia(P=0.008)
- Finally, use of butter in daily cooking or meals was associated with 2.7-times higher odds of having ACS, after adjusting for age and sex (OR=2.7, P<0.001). No associations were observed between cheese or low fat dairy intake and age, sex or other clinical characteristics of the participants.

Author Conclusion:

Dairy consumption seems to offer significant protection against CHD, irrespective of various clinical, lifestyle and other characteristics of the participants.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	???
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	No
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	No
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	N/A
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	N/A
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes